REMARKS

The Invention

The invention features methods of repairing scarred myocardial tissue by implanting into the scar tissue mesenchymal stem cells or cells derived from mesenchymal stem cells to improve cardiac function.

The Office Action

Claims 1-13 and 25-30 are pending. All of the claims stand rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness, under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,736,396 ("the '396 patent"), and under 35 U.S.C. § 103(a) as being obvious over U.S. Patent No. 5,602,301, Robinson et al. ("Robinson"), Murry et al. ("Murry" and/or WO99/03973 ("WO039"), in view of Wakitani et al. ("Wakitani") and the '396 patent. These rejections are addressed below, in the order in which they appear in the Office Action.

Rejections Under 35 U.S.C. § 112, second paragraph

Claims 1-13 and 25-30 are rejected under 35 U.S.C. § 112, second paragraph, for indefiniteness for lacking proper antecedent basis due to the omission of the word "myocardial." Applicants have addressed this rejection by amendment of claims 1 and 25.

Claims 3, 12, 29, and 30 further are rejected for indefiniteness for being in the passive voice. This rejection has been rendered moot by cancellation of claims 3, 12, 29, and 30.

Claim 13 is rejected for indefiniteness because, according to the Examiner, "it is uncertain what product/composition is encompassed by this phrase." In particular, the Examiner enquires, "does the phrase 'non-passaged' encompass at least one passage to separate hematopoietic cells?" Applicants respectfully traverse this rejection.

The Examiner is directed to page 6, lines 7-13, where passaging is defined as a subculturing step. From this definition, one in the art would readily understand that cells that have not been passaged are those that have been purified by increasing the percentage of mesenchymal stem cells but have not been subjected to this subculturing step. In view of the foregoing, applicants submit that claim 13 is definite.

In addition to the above rejections, the Examiner states that "5-aza treatment appears to be critical to the present invention" and thus "the method appears to encompass incorporation of additional active step(s) or element(s) which is (are) omitted in the claims, such omission amounting to a gap." Applicants respectfully disagree. In the specification, Applicants describe experiments in which mesenchymal stem cells not treated with 5-aza were shown to be capable of differentiating into myogenic-like cells *in vivo* (see, e.g., page 9, lines 17-20). In view of the positive results obtained using methods that do not employ 5-aza, Applicants request that this rejection be withdrawn.

Rejections Under 35 U.S.C. § 102(b)

Claims 1-13 and 25-30 are rejected under 35 U.S.C. § 102(b) for anticipation by the '396 patent. The Examiner notes that this rejection is due to the omission of the word "myocardial." Applicants have amended claims 1 and 25 (the two independent claims rejected for anticipation), and this rejection may now be withdrawn.

Rejections under 35 U.S.C. § 103(a)

Claims 1-13 and 25-30 are rejected as being obvious over the '301 patent, Robinson, Murry, and/or WO039, in view of Wakitani and the '396 patent. According to the Examiner, the primary references (the '301 patent, Robinson, Murry, and WO039), teach a method for repairing myocardial tissues by transplanting skeletal myoblasts into damaged or injured myocardial tissues, and the substitution of mesenchymal stem cells for skeletal myoblasts would be obvious in view of Wakitani and the '396 patent.

Claims 1 and 25, the independent claims rejected for obviousness, have been amended to recite that mesenchymal stem cells are transplanted into the myocardial scar tissue, i.e., the fibrous tissue that replaces the necrotic muscle following muscle resorption. None of the cited references teaches or suggests transplanting cells of any kind into myocardial scar tissue. In view of this amendment of claims 1 and 25, the rejection of claims 1-13 and 25-30 for obviousness may now be withdrawn.

Conclusion

Enclosed is a petition to extend the period for replying for three months, to and including April 9, 2002. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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Version With Markings to Show Changes Made

1. (Amended) A method for repairing [treating damaged or] scarred myocardial tissue, said method comprising administering to [said damaged or scarred] myocardial scar tissue a cellular suspension containing mesenchymal stem cells, wherein administration of said cells to said myocardial scar tissue repairs said scarred myocardial tissue.

13. (Amended) The method of claim 1, wherein said mesenchymal stem cells [are] have not been passaged.

25. (Twice Amended) A method for repairing [treating damaged or] scarred myocardial tissue, said method comprising administering to [said damaged or scarred] myocardial scar tissue a cellular suspension comprising mesenchymal stem cells that have been cultured *ex vivo*.